Living donor liver transplantation (LDLT) has become a routine surgical procedure for a patient with an end-stage liver disease such as severe deterioration of liver function. Due to the scarcity of pediatric and cadaveric donors, LDLT has been practiced increasingly in countries where living donors are practically the primary sources of organs for donation [1-5].

Estimation of graft weight (GW) is important to both recipients and donors for safe and successful LDLT. The ratio of an estimated GW to a recipient’s body weight is crucial for the recipient to prevent post-transplant complications due to small-for-size syndrome [6-13] or large-for-size syndrome [8, 14]. For example, use of a small-for-size graft can result in lower graft survival due to enhanced parenchymal cell injury and reduced metabolic and synthetic capacity [8], while use of a large-for-size graft can cause an increased risk of vascular complications, immunological impairments [8] and respiratory failure [14]. In contrast, loss of excessive liver tissue for a donor can lead to a high risk of postoperative liver failure [15, 16]. For example, Schindl et al. [15] reported that postoperative serious hepatic dysfunction often occurs if the ratio of residual to total functional liver volume (TFLV = entire liver volume − tumor volume) is smaller than 26.6%.

Right lobe GW has been directly estimated by computed tomographic (CT) volumetry, however, there is a tendency that CT volumetry overestimates GW. Right lobe GW is often considered equal to right lobe graft volume (GV) estimated by CT volumetry with an assumption of liver density = 1.00 g/ml [17, 18]. However, several studies reported that right lobe GW estimated by CT volumetry is larger than the intraoperatively measured right lobe GW [19-25]. The major causes of CT volumetric error include intraoperative drainage of blood [26] and actual liver density different from 1.00 g/ml (e.g., Yu et al. [27] reported 1.04 g/ml of liver density).

Right lobe GW estimation formulas have been established using right lobe GV with veins (GVw\_veins) including portal vein and hepatic vein by sacrificing accuracy due to inclusion of the blood volume in the intrahepatic veins in the preoperatively measured CT volume of the graft. Lemke et al. [21] and Yoneyama et al. [28] developed GVw\_veins-based GW estimation formulas for the German (GW = 143.704 + 0.678 × GVw\_veins; adjusted *R*2 = 0.76) and the Japanese (GW = 0.84 × GVw\_veins; adjusted *R*2 = 0.52), respectively. However, the accuracy of a GVw\_veins-based GW estimation formula is sacrificed because an intraoperatively measured GW excludes the weight of blood in the intrahepatic veins.

Formulas established by right lobe GV without veins (GVw/o\_veins = GVw\_veins – blood volume in the intrahepatic veins) are needed for right lobe GW estimation with better accuracy. Kim et al. [25] and Mokry et al. [29] developed right lobe GVw/o\_veins-based GW estimation formulas for the Korean (GW = 88.5117 + 0.8815 × GVw/o\_veins; adjusted *R*2 = 0.84) and the German (GW = 28.0 + 1.01 × GVw/o\_veins; adjusted *R*2 = 0.92), respectively. Kim et al. [25] reported that the percentage of absolute error of the GVw/o\_veins-based formula was 5.0%, whereas that of the GVw\_veins-based formula was 10.2%. However, their GVw/o\_veins-based formula still needs to be improved since the percentage of absolute error larger than 10% occurred in 2 out of 88 cases in their study [25]. On the other hand, Mokry et al. [29] reported an opposite result (the error ratio of the GVw/o\_veins-based formula was −6.5%, whereas that of the GVw\_veins-based formula was −2.7%) without providing information of percentage of absolute error and the number of cases of which percentage of absolute error > 10%.

The present study was intended to develop a more accurate formula for right lobe GW estimation using right lobe GVw/o\_veins measured by CT volumetry and compare its estimation accuracy with those of existing formulas. GW estimation models were established using CT volumetric data of Korean patients and their accuracy performance was assessed in terms of absolute error, percentage of absolute error, and number of cases of which percentage of absolute error > 10%.

**MATERIALS AND METHODS**

**Patient Data**

Preoperative abdominal CT images and intraoperatively measured GWs of 40 right lobe graft donors (8 females and 32 males; age = 29.6 ± 10.3 years) were provided by Pusan National University Yangsan Hospital (PNUYH) for establishment of GW estimation formulas in the present study. Additionally, data of 20 right lobe graft donors (6 females and 14 males; age = 24.1 ± 6.9 years) from PNUYH and 23 right lobe graft donors (5 females and 18 males; age = 29.6 ± 10.8 years) from Chonbuk National University Hospital (CNUH) were provided for cross-validation of GW estimation formulas. The present study was approved by the IRBs at PNUYH and CNUH.

**CT Imaging**

CT images were obtained using a 128-row multidetector CT scanner (SOMATOM Definition AS+; Siemens, Forchheim, Germany). Potential liver donors were fasted for more than 6 hours before CT scanning. CT scanning was performed while the donor held a breath at the end of inspiration. After obtaining CT images without a contrast medium, 120 to 130 ml of Iopromide (Ultravist 370; Schering, Berlin, Germany) was administered at a flow rate of 3 ml/sec using a mechanical injector followed by triphasic CT scanning during the arterial, portal, and delayed phases. An automatic bolus-tracking system (CARE Bolus; Siemens, Forchheim, Germany) was used to trigger data acquisition after enhancement of the descending aorta reached a threshold of 100 Hounsfield Units. The scanning and reconstitution parameters were as follows: detector collimation = 128 × 1.5 mm for unenhanced scanning and 128 × 0.75 mm for enhanced scanning; pitch value (table feed per gantry rotation divided by collimated beam width) = 0.6; gantry rotation time = 0.5 sec; and slice thickness = 3 mm.

**Preoperative CT Volumetric Measurement**

***Right Lobe Graft Volume with Veins***

Two LDLT expert surgeons measured the right lobe GVw\_veins of each donor with CT volume data obtained in the delayed phase in two steps: (1) liver extraction and volumetry and (2) right lobe graft resection and volumetry (Figure 1.a) by Dr. Liver™ (Humanopia, Inc., Pohang, South Korea). In the liver extraction and volumetry step, liver was extracted from CT volume data based on selected multiple seed points using a hybrid semi-automatic liver extraction method [30] with a high accuracy (97.6%) in CT volumetry. The extrahepatic portal vein and inferior vena cava were automatically excluded from the extracted liver. In the right lobe graft resection and volumetry step, the extracted liver was interactively segmented into left and right lobes by a curved resection plane. Resection planes for liver segmentation at the two hospitals differed from each other due to difference in surgical technique applied. In case of PNUYH, the resection plane passed through the center of the inferior vena cava, the middle hepatic vein, and the middle of the gallbladder bed [31]. In case of CNUH, the resection plane passed through the center of the inferior vena cava, the right side of the middle hepatic vein, and the middle of the gallbladder bed. The total liver volume of the donor with veins (LVw\_veins) and GVw\_veins were calculated using the summation-of-area method [32].

***Right Lobe Graft Volume without Veins***

The measurement process of right lobe GVw/o\_veins was similar to that of right lobe GVw\_veins except that two more steps (extraction of veins and subtraction of veins from the liver) were added to exclude veins from the extracted liver (Figure 1.b.). After liver extraction with Dr. Liver, the intrahepatic veins including portal and hepatic veins were semi-automatically extracted by a region growing method using multiple seed points interactively selected by surgeons from two to three CT slices. Then the intrahepatic veins were subtracted from the extracted liver regions to obtain liver regions without veins. Lastly, the liver regions without veins were divided into left and right lobes by a curved resection plane as explained before and the total liver volume without veins (LVw/o\_veins) and GVw/o\_veins were calculated.

[Insert Figure 1 about here]

**Intraoperative Measurement of Actual Graft Weight**

A liver graft was flushed by a surgeon at the back table with histidine-tryptophan-ketoglutarate solution (Custodiol; Köhler Chemie, Alsbach-Hähnlein, Germany). Then the graft was trimmed and weighed.

**Statistical Analysis**

Intraoperative measurements of right lobe GW were plotted against preoperative estimates of right lobe GVw\_veins and GVw/o\_veins, respectively. Regression formulas were established to describe the relationships between right lobe GW and GVw\_veins/GVw/o\_veins. A residual analysis was conducted to assess the adequacy of fit of the regression models. The two-sample *t*-test was conducted to find if significant differences exist between different gender (male vs. female) and age groups (under 30 vs. over 40 years) in terms of GW estimation error. All statistical analysis was conducted using Minitab v. 14 (Minitab, Inc., USA) at ** = 0.05.

**RESULTS**

**Measurements of Right Lobe Graft Weight, Graft Volumes with and without Veins**

The average ± SD of intraoperatively measured right lobe GW was 732.9 ± 136.4 g (range = 471 to 1033 g). The average ± SD of preoperative right lobe GVw\_veins was 851.0 ± 164.6 ml (range = 522 to 1135 ml), whereas the average ± SD of preoperative right lobe GVw/o\_veins was 746.1 ± 140.2 ml (range = 462 to 1024 ml).

**Regression Formulas for Right Lobe Graft Weight Estimation**

GW estimation formulas based on GVw\_veins and GVw/o\_veins were established in the present study. The GVw/o\_veins-based formula (GW = 29.1 + 0.943 × GVw/o\_veins, adjusted *R*2 = 0.94, *p* < .05; Figure 2.a) was found superior to the GVw\_veins-based one (GW = 74.7 + 0.773 × GVw\_veins, adjusted *R*2 = 0.87, *p* < .05; Figure 2.b).

[Insert Figure 2 about here]

**Cross Validation Results**

The proposed GVw/o\_veins-based formula achieved the highest adjusted *R*2 value and accuracy in GW estimation compared with the existing formulas (Table 1). The proposed GVw/o\_veins-based formula was compared with the existing formulas using data (*n* = 43) from the two centers for validation in terms of absolute error (AE, g) and percentage of absolute error (PAE, %). AE defines the absolute difference between GW estimated by a regression formula and corresponding GW intraoperatively measured. PAE is the ratio of AE to intraoperatively measured GW. The GVw\_veins-based formula established in the present study showed similar performance to those reported by Lemke et al. and Yoneyama et al. The proposed GVw/o\_veins-based formula was found superior to all the GVw\_veins-based and GVw/o\_veins-based formulas in terms of adjusted *R*2, AE, and PAE. The superiority of the proposed GVw/o\_veins-based formula in GW estimation was also observed in cross validation. Note that the proposed GVw/o\_veins-based formula did not have any cases of which PAE > 10%. No significant differences were found between different gender (male vs. female: *t*(7) = .48, *p* = .648 for AE; *t*(6) = .21, *p* = .843 for PAE) and age groups (under 30 vs. over 40 years: *t*(4) = −0.54, *p* = .619 for AE; *t*(5) = −0.53, *p* = .621 for PAE).

[Insert Table 1 about here]

**DISCUSSION**

The present study developed regression formulas based on preoperatively measured right lobe GVw/o\_veins and GVw\_veins to estimate right lobe GW. The GVw\_veins-based formulas sacrifice accuracy in GW estimation because the graft procured intraoperatively is weighed after the blood in the liver is drained. By excluding the volume of the veins from GV, GW could be estimated more accurately in the present study.

The proposed GVw/o\_veins-based formula in the present study was found superior to the existing GVw\_veins- and GVw/o\_veins-based formulas in terms of adjusted *R*2 and accuracy (AE and PAE). The proposed GVw/o\_veins-based formula showed the largest adjusted *R*2 (= 0.94) and smallest AE (= 16.3 ± 12.6 g for PNUYH data and 21.5 ± 16.5 g for CNUH data) and PAE (= 2.6 ± 2.2% for PNUYH data and 3.0 ± 2.3% for CNUH data; all PAEs < 10%).

The cross validation results of the present study support the superiority of the proposed GVw/o\_veins-based formula. Lemke et al. [21] reported that the error ratio of their GVw\_veins-based formula in GW estimation was 20.5% ± 10.8%. The possible causes of the substantial error were listed as follows: (1) lack of accuracy in liver segmentation, (2) discrepancy among examination techniques and examiners, and (3) intraoperative drainage of liquid such as blood from the liver. The present study could minimize the effects of the possible causes of errors in GW estimation and achieved a significantly small error ratio (= 3.0% ± 2.3%) using GVw/o\_veins. Firstly, the present study applied a hybrid semi-automatic liver extraction method [30] which has a high accuracy (97.6%) for preoperative CT volumetric measurement. Secondly, the consistency between the right lobe graft preoperatively identified using Dr. Liver and the right lobe graft intraoperatively harvested was maximized in the present study because the same surgeon conducted surgery planning for LDLT using Dr. Liver. Lastly, this study minimized the effect of intraoperative drainage of blood on GW estimation by excluding the volume of blood vessels from right lobe GV in surgery planning.

Use of the GVw/o\_veins-based formula requires 2 to 3 min more than that of the GVw\_veins-based formula due to reconstruction and exclusion of veins from right lobe GV. For the GVw\_veins-based formula, measurement of a preoperative GVw\_veins took 3 to 5 min by Dr. Liver including liver extraction (2 to 3 min) and graft resection (1 to 2 min). For the GVw/o\_veins-based formula, measurement of a GVw/o\_veins took 2 to 3 min more due to additional steps to extract veins and exclude the volume of veins from right lobe GV.

Future study is needed to examine the generalizability of the proposed GVw/o\_veins-based regression model for GW estimation. Data of populations other than Koreans and/or those collected from various medical centers can be analyzed to examine the effects of race and GV measurement protocol on the accuracy of GW estimation.

**CONCLUSIONS**

GVw/o\_veins-based formula is preferred to GVw\_veins-based formula in GW estimation. Accurate preoperative CT volumetry and matching between planned and real surgical cutting lines are crucial in establishment of an accurate GW estimation formula.

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**REFERENCES**

[1] Pichlmayr R, Ringe B, Gubernatis G, Hauss J, Bunzendahl H. Transplantation of a donor liver to 2 recipients (splitting transplantation)-a new method in the further development of segmental liver transplantation. Langenbecks Arch Chir 1988;373:127–130.

[2] Kawasaki S, Makuuchi M, Matsunami H, Hashikura Y, Ikegami T, Nakazawa Y, et al. Living related liver transplantation in adults. Ann Surg 1998;227:269–74.

[3] Tanaka K, Uemoto S, Tokunaga Y, Fujita S, Sano K, Nishizawa T, et al. Surgical techniques and innovations in living related liver transplantation. Ann Surg 1993;217:82–91.

[4] Lee SG, Park KM, Lee YJ, Hwang S, Choi DR, Ahn CS, et al. 157 adult-to-adult living donor liver transplantation. Transplant Proc 2001;33:1323–5.

[5] Chen CL, Fan ST, Lee SG, Makuuchi M, Tanaka K. Living-donor liver transplantation: 12 years of experience in Asia. Transplantation 2003;75(3 Suppl):S6–11.

[6] Inomata Y, Kiuchi T, Kim I, Uemoto S, Egawa H, Asonuma K, et al. Auxiliary partial orthotopic living donor liver transplantation as an aid for small-for-size graft in larger recipients. Transplantation 1999;67:1314–9.

[7] Sakamoto S, Uemoto S, Uryuhara K, Kim I, Kiuchi T, Egawa H, et al. Graft size assessment and analysis of donors for living donor liver transplantation using right lobe. Transplantation 2001;71:1407–13.

[8] Kiuchi T, Kasahara M, Uryuhara K, Inomata Y, Uemoto Y, Asonuma K, et al. Impact of graft size mismatching on graft prognosis in liver transplantation from living donors. Transplantation 1999;67:321–7.

[9] Ben-Haim M, Emre S, Fishbein TM, Sheiner PA, Bodian CA, Kim-Schluger L, et al. Critical graft size in adult-toadult living donor liver transplantation: impact of the recipient’s disease. Liver Transpl 2001;7:948–53.

[10] Heaton N. Small-for-size liver syndrome after auxiliary and split liver transplantation: donor selection. Liver Transpl 2003;9:S26–8.

[11] Kiuchi T, Tanaka K, Ito T, et al. Small-for-size graft in living donor liver transplantation: how far should we go? Liver Transpl 2003;9:S29–35.

[12] Nishizaki T, Ikegami T, Hiroshige S, et al. Small graft for living donor liver transplantation. Ann Surg 2001;233:575–80.

[13] Sugawara Y, Makuuchi M, Takayama T, et al. Small-for-size grafts in living-related liver transplantation. J Am Coll Surg 2001;192:510–3.

[14] Levesque E, Duclos J, Ciacio O, Adam R, Castaing D, Vibert E. Influence of larger graft weight to recipient weight on the post-liver transplantation course. Clin Transplant 2013;27:239–47.

[15] Schindl MJ, Redhead DN, Fearon KC, Garden OJ, Wigmore SJ. The value of residual liver volume as a predictor of hepatic dysfunction and infection after major liver resection. Gut 2005;54:289–96.

[16] Ferrero A, Viganò L, Polastri R, Muratore A, Eminefendic H, Regge D, et al. Postoperative liver dysfunction and future remnant liver: where is the limit? Results of a prospective study. World J Surg 2007;31:1643–51.

[17] Lemke AJ, Hosten N, Neumann K, et al. CT volumetry of the liver before transplantation. Rofo 1997;166:18–23.

[18] Van Thiel DH, Hagler NG, Schade RR, et al. In vivo hepatic volume determination using sonography and computed tomography: validation and a comparison of the two techniques. Gastroenterology 1985;88:1812–7.

[19] Hiroshige S, Shimada M, Harada N, et al. Accurate preoperative estimation of liver-graft volumetry using three-dimensional computed tomography. Transplantation 2003;75:1561–4.

[20] Gondolesi GE, Yoshizumi T, Bodian C, et al. Accurate method for clinical assessment of right lobe liver weight in adult living-related liver transplant. Transplant Proc 2004;36:1429–33.

[21] Lemke AJ, Brinkmann MJ, Schott T, et al. Living donor right liver lobes: preoperative CT volumetric measurement for calculation of intraoperative weight and volume. Radiology 2006;240:736–42.

[22] Nakayama Y, Li Q, Katsuragawa S, et al. Automated hepatic volumetry for living related liver transplantation at multisection CT . Radiology 2006;240:743–8.

[23] Radtke A, Sotiropoulos GC, Nadalin S, et al. Preoperative volume prediction in adult living donor liver transplantation: how much can we rely on it? Am J Transplant 2007;7:672–9.

[24] Yuan D, Chen K, Li B, Yan L, Wei Y. Accurate and reasonable method for estimation of graft volume in living donor liver transplantation. Transplantation 2008;86:1011–2.

[25] Kim KW, Lee J, Lee H, Jeong WK, Won HJ, et al. Right lobe estimated blood-free weight for living donor liver transplantation: accuracy of automated blood-free CT volumetry-preliminary results. Radiology 2010;256:433–40.

[26] Salvalaggio PR, Baker TB, Koffron AJ, et al. Liver graft volume estimation in 100 living donors: measure twice, cut once. Transplantation 2005;80:1181–5.

[27] Yu HC, You H, Lee H, et al. Estimation of standard liver volume for liver transplantation in the Korean population. Liver Transpl 2004;10:779–83.

[28] Yoneyama T, Asonuma K, Okajima H, Lee KJ, Yamamoto H, Takeichi T, et al. Coefficient factor for graft weight estimation from preoperative computed tomography volumetry in living donor liver transplantation. Liver Transpl 2011;17:369–72.

[29] Mokry T, Bellemann N, Müller D, Bermejo JL, Klauß M, Stampfl U, et al. Accuracy of estimation of graft size for living-related liver transplantation: first results of a semi-automated interactive software for CT-volumetry. PLoS ONE 2014;9:e110201.

[30] Yang X, Yu HC, Choi Y, Lee W, Wang B, Yang J, et al. A hybrid semi-automatic method for liver segmentation based on level-set methods using multiple seed points. Computer Methods and Programs in Biomedicine 2014;113:69–79.

[31] de Villa VH, Chen CL, Chen YS, et al. Right lobe living donor liver transplantation: addressing the middle hepatic vein controversy. Ann Surg 2003;238:275–82.

[32] Heymsfield SB, Fulenwider T, Nordlinger B, Barlow R, Sones P, Kutner M. Accurate measurement of liver, kidney, and spleen volume and mass by computerized axial tomography. Ann Intern Med 1979;90:185–7.

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| --- | --- | --- | --- |
| Models | Adjusted*R*2 | PNUYH Data (*n* = 20) | CNUH Data (*n* =23) |
| Absolute Error (AE; g) | Percentage of AE (PAE = AE/GW; %) | # cases of PAE > 10%(%) | AE(g) | PAE(%) | # cases of PAE > 10%(%) |
| Mean(SD) | SE | Mean(SD) | SE | Mean(SD) | SE | Mean(SD) | SE |
| The present study |  |  |  |  |  |  |  |  |  |  |  |
| GW = 29.1 + 0.943 × GVw/o\_veins | 0.94 | 16.3(12.6) | 2.8 | 2.6(2.2) | 0.5 | None | 21.5(16.5) | 3.4 | 3.0(2.3) | 0.5 | None |
| GW = 74.7 + 0.773 × GVw\_veins | 0.87 | 35.0(25.1) | 5.6 | 5.4(3.9) | 0.9 | 2(10.0%) | 41.8(33.9) | 7.1 | 5.8(4.6) | 1.0 | 6(26.1%) |
| Lemke et al.’s formula |  |  |  |  |  |  |  |  |  |  |  |
| GW = 143.7 + 0.678 × GVw\_veins | 0.76 | 36.6(22.5) | 5.0 | 5.8(4.1) | 0.9 | 3(15.0%) | 45.5(32.9) | 6.9 | 6.1(4.1) | 0.9 | 4(17.4%) |
| Yoneyama et al.’s formula |  |  |  |  |  |  |  |  |  |  |  |
| GW = 0.84 × GVw\_veins | 0.52 | 34.2(26.4) | 5.9 | 5.0(3.5) | 0.8 | 2(10.0%) | 42.0(36.8) | 7.7 | 5.7(4.9) | 1.0 | 3(13.0%) |
| Mokry et al.’s formula |  |  |  |  |  |  |  |  |  |  |  |
| GW = 28.0 + 1.01 × GVw/o\_veins | 0.92 | 50.2(18.5) | 4.1 | 7.8(3.3) | 0.7 | 4(20.0%) | 55.0(24.6) | 5.1 | 7.7(3.6) | 0.8 | 6(26.1%) |
| Kim et al.’s formula |  |  |  |  |  |  |  |  |  |  |  |
| GW = 88.5117 + 0.8815 × GVw/o\_veins | 0.84 | 25.6(20.5) | 4.6 | 4.4(3.9) | 0.9 | 2(10%) | 28.3(17.8) | 3.7 | 4.1(2.7) | 0.6 | 1(4.3%) |

Table 1. Validation results of graft weight (GW) estimation models

GVw\_veins: graft volume with veins, GVw/o\_veins: graft volume without veins, SD: standard deviation, SE: standard error

**Figure Legends**

Figure 1. Right lobe graft volume measurement procedure: (a) graft volume with veins and (b) graft volume without veins.

Figure 2. Relationships between intraoperatively measured graft weight (GW) and preoperatively estimated graft volume (GV) (*n* = 40 cases): (a) GW vs. GVw\_veins (GV with veins) and (b) GW vs. GVw/o\_veins (GV without veins).



Figure 1. Right lobe graft volume measurement procedure: (a) graft volume with veins and (b) graft volume without veins.

|  |  |
| --- | --- |
|  |  |
| (a) | (b) |

Figure 2. Relationships between intraoperatively measured graft weight (GW) and preoperatively estimated graft volume (GV) (*n* = 40 cases): (a) GW vs. GVw\_veins (GV with veins) and (b) GW vs. GVw/o\_veins (GV without veins).